REMARKS

Claims 1-14 were rejected under 35 U.S.C. §103(a) as being unpatentable over US Pat. 5,860,931 (Chandler). Claim 1 describes a method of obtaining an ultrasound perfusion image of tissues perfused with blood containing microbubbles, the method comprising transmitting a plane wave of microbubble-destroying ultrasound into the tissues, the plane wave of microbubble-destroying ultrasound encompassing a first area of the tissues, the microbubble-destroying ultrasound having an intensity that is sufficient to destroy microbubbles in the tissues that are insonified by the microbubble-destroying ultrasound; repetitively transmitting a plurality of beams of imaging ultrasound into the tissues, each beam of imaging ultrasound having a second area that is smaller than the first area, the imaging ultrasound having an intensity that is substantially insufficient to destroy microbubbles in the tissues that are insonified by the imaging ultrasound; receiving reflections from each of the transmitted imaging ultrasound beams in respective receive beams, each of the receive beams having a third area that is smaller than the first area; and processing the received reflections over a sufficient period to allow re-perfusion of the tissues to provide an ultrasound perfusion image. The use of a plane wave of ultrasound to destroy the microbubbles quickly eliminates microbubbles from the tissues under examination and ensures that the subsequent reperfusion of the tissues can be assessed from a known contrast-destroyed baseline. In the prior art, which used focused beams to sequentially destroy microbubbles along each beam path, some reperfusion could start in the early beam directions while microbubble destruction was still underway in the directions of the later-transmitted beams. Thus, there was no common baseline throughout the tissues of microbubble destruction, as different beam locations could already be experiencing reperfusion at the time the low-level acquisition of microbubble measurement commenced. A plane wave can destroy the microbubbles in a broad expanse of tissue in one transmission, enabling accurate measurement of the rate of reperfusion throughout the tissue.

Chandler is assessing reperfusion at a specific point in an image field. After the patient has been perfused with contrast agent and an equilibrium of contrast agent is established, Chandler measures this equilibrium level at a region of interest. He then transmits highly focused beams to destroy the microbubbles in a second region which is preferably fully overlapping with the region of interest. Chandler does not use a plane wave, but instead uses "low F number beams that have very high degrees of focus." See column 4 at lines 34-35. The reason he uses highly focused beams is that he is concerned

with the uniformity of microbubble destruction (col. 5, line 65 to col. 6, line 6). But he realizes that the most complete microbubble destruction will occur where the beam energy is concentrated with the greatest intensity at the beam focus. So he sets his focus point at the region of interest which provides maximum contrast agent destruction there, with the beam intensity rising above and then falling below the destruction threshold before and after the focus. See col. 6, lines 7-16. This provides a "well-defined contrast-agent desctruction region within which to conduct the perfusion measurements." (col. 5, lines 62-65). Thus it is seen that Chandler does not show or suggest the use of a plane wave for microbubble destruction, but a sequence of highly focused beams directed at a specific region of interest. Chandler's approach provides complete and uniform destruction at his specific region of interest, but he is only able to make his measurements at a very specific point in the image field. To make subsequent measurements at other points, he must re-select a new region of interest again and again and re-steer and re-focus his beams at these new regions until he has acquired the desired set of measurements. With the present invention, measurements can be made at different points in the wide area covered by retransmission of the same plane wave, making the clinician's task much simpler. Futhermore, Chandler overlooks the fact that the contrast agent is generally introduced in the clinical setting in a "bolus" from an injection. The contrast measurements must be taken very quickly as the time of maximum concentration of the bolus at any particular location in the body is short. For these reasons it is respectfully submitted that Claim 1 and its dependent Claims 4, 7, and 8 are patentable over Chandler.

Claim 11 describes a method of obtaining an ultrasound perfusion image of tissues perfused with blood containing microbubbles, the method comprising using ultrasound to simultaneously destroy substantially all of the microbubbles in the tissues over a first area; and repetitively using ultrasound transmitted and received in a plurality of second areas that substantially encompasses the first area to obtain an indication of the quantity of microbubbles in the tissues that are intact over a re-perfusion time, each of the second areas being smaller than the first area, wherein the act of using ultrasound to simultaneously destroy substantially all of the microbubbles in the tissues over a first area comprises using a plane-wave beam of ultrasound to simultaneously destroy substantially all of the microbubbles in the tissues over the first area. It is seen that Claim 11 calls for the use of a plane-wave beam of ultrasound to simultaneously destroy substantially all of the microbubbles in the tissues over the first area. As previously mentioned, the use of a plane-wave enables reperfusion measurements to start from a common baseline of microbubble

depletion over the entire area. As discussed above, Chandler does not show or suggest the use of a plane-wave, but instead uses highly focused beams and repetitively so in order to assure uniform contrast agent destruction in his region of interest at the focal point. For this reason it is respectfully submitted that Claim 11 and its dependent Claim 12 are patentable over Chandler.

Claim 3 describes a method of obtaining an ultrasound perfusion image of tissues perfused with blood containing microbubbles, the method comprising transmitting a plurality of broad beams of microbubble-destroying ultrasound into the tissues, the steering directions of the beams of microbubble-destroying ultrasound encompassing a first area of the tissues, the microbubble-destroying ultrasound having an intensity that is sufficient to destroy microbubbles in the tissues that are insonified by the microbubble-destroying ultrasound; repetitively transmitting a plurality of beams of imaging ultrasound into the tissues, each beam of imaging ultrasound having a second area that is smaller than the first area, the imaging ultrasound having an intensity that is substantially insufficient to destroy microbubbles in the tissues that are insonified by the imaging ultrasound; receiving reflections from each of the transmitted imaging ultrasound beams in respective receive beams, each of the receive beams having a third area that is smaller than the first area; and processing the received reflections over a sufficient period to allow re-perfusion of the tissues to provide an ultrasound perfusion image, wherein the act of transmitting broad beams of microbubble-destroying ultrasound into the tissues comprises sequentially transmitting differently steered beams of microbubble-destroying ultrasound at a rate that is sufficiently high that subsequent beams are transmitted before a previously transmitted beam of microbubble-destroying ultrasound has been fully reflected from the tissues. As explained in paragraphs [0021] - [0022] of the present specification, microbubbles can be destroyed very quickly by transmitting broad beams without waiting for the full round-trip transit time between each beam that is necessary for echo reception. Since it is not necessary to receive the echoes in response to any of the microbubble-destruction beams, the broad beams can be transmitted in a quick burst that destroys the microbubbles and readies the tissues in the image field for reperfusion imaging. These multiple successive or simultaneous beams are differently steered to different areas of the image field, enabling the full image field to be depleted of microbubbles after just a few rapid transmissions. Paragraph [0022] gives the example of a burst of three successive or simultaneous destruction beams.

Chandler uses a continuous transmission of groups of destructive beams, with the number of beams of the beam pattern of each group being sufficient to cover the region of

interest. Col. 8, lines 55-58. Since Chandler's technique begins with non-destructive imaging of the equilibrium contrast level of contrast, the transmissions first are at a low level. He then turns up the beam gain until he observes the destruction of microbubbles throughout his region of interest. See col. 9, lines 11-20. Since Chandler is observing an image at this time, he is waiting for a transmit-receive interval following each beam transmission to receive the echoes he needs to form an image. Consequently Chandler is not transmitting destructive beams at a rate such that subsequent destructive beams are transmitted before echoes are fully received from his region of interest. He must wait for these echoes before transmitting a subsequent beam, as he needs these echoes to form the image that must be observed while adjusting the gain. Accordingly it is respectfully submitted that Chandler does not show or suggest the method of Claim 3 or its dependent Claims 5, 9 and 10.

The patents which were cited but, though pertinent, were not applied have been reviewed and are not believed to affect the patentability of the above claims.

In view of the foregoing discussion it is respectfully submitted that Claims 1, 3-5, and 7-12 are patentable over Chandler. Accordingly it is respectfully requested that the rejection of these claims under 35 U.S.C. §103(a) be withdrawn.

In light of the foregoing remarks, it is respectfully submitted that this application is now in condition for allowance. Favorable reconsideration is respectfully requested.

Respectfully submitted,

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